CANCER OF THE GALL-BLADDER AND DUCTS.

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THE attention of the writer was drawn more particularly to this subject by the occurrence of four proven and two suspected cases of primary carcinoma of the biliary ways, in 25 cases of gall-bladder disease, in his private practice during the past few years. This percentage of cases of malignancy was so large that it excited surprise. The literature in this country is quite limited, only a few articles having appeared in American journals, notably those of Musser and Mayo, while the foreign literature is very voluminous. It seems, therefore, that the attention of the profession should be directed to the subject so that these cases may receive earlier and perhaps more successful effort for their relief. The outlook for them is so gloomy that one turns to the study of this condition with reluctance and with little hope of any lasting or noteworthy results. That the subject is of sufficient importance to demand consideration is shown by the increasing frequency with which cases are being observed. McNeal[1] in 1836 mentions carcinoma of the ampulla of Vater, and cancer of the gall-bladder was considered by Durand-Fardel in 1840, yet it was not until the classic works of Zenker in 1889 and of Courvoisier in 1890 that the subject received the consideration it deserved. Zenker collected 48 cases, of which eight were taken from the pathologic institute of Erlangen from 1852 to 1889. As he says eight cases, distributed over such a long time, is certainly a small number, when we consider that six cases followed one another in Breslau during 1876-77. In the pathologic institute in Helsingfors six cases of cancer of the gall-bladder and ducts were found in 3,775 autopsies in thirty years from 1858-1888. On the other hand, Petersen of the surgical clinic of Heidelberg, found 34 cases of carcinoma among 168 operations for diseases of the gall-bladder, a rather alarming percentage; larger even than my own. Gersuny states that carcinoma forms one-fifth of all cases of gall-bladder operations.

G. R. Slade[2] makes some interesting and surprising statements concerning the frequency with which carcinoma of the gall-bladder was found in cases of stone examined post mortem. In 2,180 consecutive necropsies, 33 were cases in which gall-stones were present in the gall-bladder or had been removed just prior to death. In 17 of these 33 cases, the stones were latent and were discovered only at autopsy. In 16 of the latent cases the wall of the gall-bladder was not thickened and its mucous membrane appeared perfectly healthy. In the remaining case, the wall of the bladder was thickened, shrunken, and closely moulded over three large stones, so that no cavity remained. Microscopical examination of this wall showed carcinoma. Of the remaining 16 cases, in which stones produced symptoms, in one the gall-bladder had been removed for cancer shortly before death; in three cases the condition was pronounced cancerous on the post-mortem table; in two of these the opinion was confirmed by the microscope, and in the third the macroscopic appearance plainly showed its malignant nature. In 12 cases the wall presented an appearance of chronic inflammatory thickening. In seven of these no microscopical examination was made, but in every one of the remaining five, histological examination showed carcinoma. Cancer was found in 30 per cent. of all (10 in 33); in 56 per cent. of all cases where stones had caused symptoms; and in 58.8 per cent. (10 in 17) of all cases in which at the autopsy the wall of the gall-bladder showed inflammatory thickening. Slade also says that these figures, though startling, probably understate the true proportion. It should be particularly noted that in this calculation the seven cases not submitted to examination by microscope have all been reckoned as non-cancerous, although to the naked eye they presented an appearance exactly similar to that of the five cases which were examined and proved cancerous. Since he began in such cases to examine the wall of the gall-bladder as a routine, he has in no instance failed to find indubitable cancer, hence he does not hesitate to suggest that had all cases been examined the percentage would have been very much nearer 100 than 58. The statement of Miodowski is somewhat corroborative of the claim of Slade. He says the external appearances are somewhat misleading and were considered by the older writers as simple induration, but the microscope will reveal their true nature. Osler states that five per cent. of all gall-stone cases show cancer, while Mayo found forty cases in 1,000 operations for gall-stone disease, and Schroeder places the ratio at 14 per cent., while my own cases show in a limited series, 16 per cent. of primary cancers of the gall-bladder and ducts.

It occurs subsequent to cholelithiasis with sufficient frequency to call attention strongly to the relation between the two conditions, and to add another weighty reason, to the many already existing, for early operation in gall-stone disease. Moynihan takes issue with Slade's figures, and says that the evidence of statistics and his own experience do not coincide with those of Dr. Slade. He says: "It is clear, I think, that the earlier stages of gall-stone disease in which operation should be practiced, so that these grave complications are avoided, is very sparingly represented in this series." He has performed over 40 cholecystectomies, two of which were done for malignancy; in 18 there was gross thickening of the wall, and in only one of these specimens was malignant disease found after careful examination. So far as he knows, only two cases have been recorded in which cancer developed after cholecystostomy had been performed. This apparently simple statement of Moynihan is worthy of consideration because of the contrast between the frequency of carcinoma of the gall-bladder in cases of cholelithiasis and its infrequency following cholecystostomy for stone. Studied in the light of Slade's statistics this statement seems to show that operation in the early stage of inflammatory thickening, or early cancer formation, may prevent the development of the clinical picture of malignancy.

The causation of carcinoma of the gall-bladder, while no clearer than that of cancer in other parts of the body, is of especial interest, since it affords an opportunity to study the effects of heredity and of irritation, two conditions well recognized as playing an important part in the development of carcinoma. Some of the English writers claim that heredity can be traced in from 11 per cent. to 17 per cent. of cases. On the other hand, Schueppel denies that it plays any part in the causation. Its exact role cannot as yet be fully determined. The relation between stones and carcinoma of the gall-bladder is so close that we are forced to conclude that the irritation which they produce must be an important factor in the production of malignancy. Budd in 1845 called attention to the frequency with which cholelithiasis and cancer of the biliary passages were associated. He, with Frerichs and others of the older writers, considered that the carcinomatous growths in the walls of the ducts caused an obstruction to the outflow of bile and thus determined the formation of stones. The facts and the weight of opinion seem to show that while carcinoma may precede the formation of stones in a few instances, especially of duct cancer, yet in the vast majority of cases the cholelithiasis precedes and in many cases is an important factor in the development of carcinoma. What part is played by infection or living organisms, in addition to that of exciting inflammation and stone formation, yet remains for solution. The acknowledgment of the importance of irritation and inflammation does not deny the possibility of a living virus being the actual determining cause. The following reasons have been advanced to support the contention that the cholelithiasis precedes the malignancy in most cases: First, the frequency with which antecedent symptoms of cholelithiasis are present; second, as pointed out by Marchand, cancer is frequently present with calculi, without any evidence of obstruction to the flow of bile; third, cancer of the gall-bladder is more often accompanied by stones than is carcinoma of the ducts, while obstruction to the flow is more often found in the latter; fourth, the neoplasm frequently has its origin in the ulcers and cicatrices in the wall of the gall-bladder and ducts, resulting from the prolonged irritation (pressure) of stones (Kelynack records two cases where stones were present in the gall-bladder although the cystic duct was occluded and the gall-bladder contained no bile. In one the stones were embedded in the tumor mass, in the other the stone lay in a depression just below a soft nodule of what was apparently the primary growth.); fifth, the frequency with which stones are found in cases of gall-bladder cancer, or in their absence, the frequency with which evidences can be discovered of their former presence; sixth, the frequency of their presence in primary cancer (95 per cent.) and their infrequency in secondary cases (15 to 16 per cent. Siegert); seventh, the large preponderance of primary cancer of these organs in women, greater even than the frequency of cholelithiasis in that sex and more than the relative frequency of cancer in men and women. Naunyn believes that half the cases diagnosed as cholelithiasis associated with chronic jaundice are either complicated with cancer or are due to this disease. The frequency with which stone is present in primary carcinoma is given by

Courvoisier as	74 in 84 cases	Jayle	23 in 30 cases
Musser	69 in 100 "	Siegert	94 in 97 "
Bodowski	40 in 40 "	Frerichs	9 in 11 "
Tiedeman	59 in 74 "	Richter	4 in 5 "
Zenker	41 in 48 "		

The average age of patients with cancer of the gall-bladder is 54.5 years, and in cancer of the ducts about the same or perhaps a fraction older.

Men and women suffer from secondary cancer of the gall-bladder with about equal frequency, while primary cases show a much greater frequency in women, who are affected four or five times as often as men. Zenker found 72.9 per cent. in women, while Naunyn found 83 per cent. in women and 17 per cent. in men. Miodowski found that in 41 cases of choledochus cancer, 26 were males and 14 females; one case gave no statement of the sex. Schultze reports 18 cases of primary disease of the hepatic duct of which twelve were males, five were females, and one not stated. These figures show an almost reverse ratio to the frequency of primary gall-bladder cancer. Miodowski gives the ages of the cases of primary duct cancer as follows, in 39 cases: From 30-40 years, 3; 40-50 years, 8; 50-60 years, 9; 60-70 years, 14; over 70 years, 5. The growth may assume the type of a columnar-celled carcinoma, a spheroidal-celled carcinoma, an adeno-carcinoma, a colloid cancer, or as claimed by some a squamous-celled epithelioma, although some deny the existence of the latter. A number of cases of epithelioma of the bile-ducts have been recorded. Treutlein[3] gives a tabulation of 108 cases of cancer of the gall-bladder reported by 29 authors, and classifies the cases clinically as scirrhous 78, as medullary 21, and as colloid nine cases. Stones were present in 99 of the cases.

The first evidence of primary carcinoma of the gall-bladder is to be found as a change in the structure of the wall. These changes are to be observed earliest in the mucous membrane and there consist of an abrasion or a loss of the epithelium in certain portions, with the formation of cicatrices as the result of inflammatory change, or the pressure of a stone or the ulceration following such pressure. Where there is no loss of epithelium, this layer may be transformed into layers of flat cells. As a result of the infiltration incidental to inflammation of the wall, and of cholelithiasis, a considerable number of the glands of the mucosa undergo atrophy. Again, as stated in Nothnagel,[4] these glands may enlarge by sending out processes, and in this manner probably compensate the loss of the destroyed glands. Or some of the glands may be displaced by the connective tissue and this, in accordance with the theory of Ribbert, may determine the development of malignancy. These cells proliferate rapidly, fill the alveoli, and invade beyond the connective-tissue limits normally present. They may undergo a mucoid or gelatinous degeneration largely as the result of imperfect nutrition, and assume the type of a gelatinous carcinoma. This form of growth is to be classified as an adeno-carcinoma. These changes may involve only a limited portion of the mucous membrane or they may be found in every part of the organ. In some cases the entire cavity of the gall-bladder, except that occupied by the stone, may be filled with this new malignant glandular tissue; such a condition was present in one of my cases. The neoplasm may produce a marked increase in the size of the gall-bladder, or again it may be accompanied by a large amount of connective-tissue formation which causes it to become shrunken, sacculated, and to fit snugly about the stone. The connective tissue of the wall shows a marked increase, probably as a result of the infiltration consequent to inflammation. The muscular tissue is hypertrophied, and finally much of it is obliterated from the contraction of the new connective tissue. When the connective tissue develops more rapidly than the epithelial elements, the neoplasm assumes the type of scirrhus. It is claimed that in some instances the epithelial cells undergo a metamorphosis into flat cells and an epithelioma results.

In the early stages, a gall-bladder, the seat of carcinoma resembles very closely macroscopically one that has been the site of a chronic inflammation. In many cases it is small, shrunken, and sacculated, while in others it is enormously increased in size. In still other instances, the exterior may give little or no evidence of a malignant growth, such condition only being discovered after incision of its wall. The growth in such cases is of small size and usually situated at the site of a cicatrix, where a gall-stone rests or has rested. The possibility of the development of a carcinoma after the escape of a stone into the intestine or after its removal by cholecystostomy must not be overlooked, although such a result is quite infrequent. The growth may spring from any portion of the wall of the bladder, may involve its entire extent, or may be situated in the cystic, hepatic, or common duct. It may be annular in form, separating one portion of the gall-bladder from the other, and each of these cavities may contain one or more stones. Sometimes each stone is found lying in a separate compartment, new tissue having occluded the cavity in many places. These changes in the structure of the wall are of necessity slow in their development, the stones often having produced symptoms through a period of years. The wall of the bladder is able in many cases to resist the encroachment of a new growth for a considerable time, thus protecting the adjacent structures from early involvement, but sooner or later the growth extends through the wall and attacks the neighboring organs. The liver is one of the first organs to be invaded secondarily. The omentum, the stomach, the intestine, and the pancreas are all liable to attack. The latter organ may escape attack, in many cases, because the obstruction in the ducts results fatally before the neoplasm has extended to it. The growth shows a marked tendency to spread along the ducts, to invade their walls, and finally to reach the liver, the duodenum, and the pancreas by continuity. The lymphatic glands in the lesser omentum may be involved, but less frequently than is usual in carcinoma. Around a gall-bladder that is the seat of such a growth we are likely to find adhesions from inflammatory change, as is noted in so many cases of chronic cholelithiasis, yet in many cases the wall is smooth and free from adhesions. The latter condition is the rule in duct cancer. As the growth progresses it may show a number of nodules in the wall and liver as well.

In the early stages the gall-bladder contains bile and usually stones; as the cystic duct is narrowed the amount of bile is lessened and finally only a bile-stained mucus may remain. In other instances the cavity may be so completely filled that no space remains for fluid. When no fluid is present the glands of the wall will be found to be almost entirely obliterated. When the growth progresses to the point of obstruction of the common or hepatic duct the tissues are promptly stained with bile coloring matter, the blood loses its power of coagulation, the ducts become dilated, sometimes to an enormous extent, and numerous gall-stones may be found in the smaller ducts of the liver. When the obstruction lies above the entrance of the cystic duct the gall-bladder is small, but when the choledochus is occluded the gall-bladder is enlarged. This is an important point in determining upon the practicability of any operative procedure, as little can be hoped when the hepatics are occluded. The kidneys very early show the pernicious effects of the toxic materials which reach them in the process of elimination. The blood, the heart, the spleen, and the general musculature of the body show marked degenerative change. Patients who have complete jaundice rarely live a year.

As a result of contractions about the portal system late in the disease, ascitic accumulation takes place into the abdomen.

Symptoms.—The careful investigation of the history of these patients will usually elicit some of the symptoms of cholelithiasis, although in some cases the first evidence of trouble is the appearance of a tumor in the right hypochondrium, or the occurrence of jaundice. The latter symptom may have been noted previously in mild degree, disappearing promptly, but when it occurs as the result of obstruction of the common or hepatic ducts it is persistent, yet may vary, now light, now dark. The temporary attacks just mentioned are often accompanied by fever, pain and vomiting, and are the result of a mild cholangeitis. When such a patient loses flesh steadily and persistently, the suspicion of malignancy is strong. In the absence of jaundice, the skin presents a peculiar sallow, anæmic appearance, which is somewhat characteristic. The appetite may be fair in the absence of jaundice, but as a rule the digestion is impaired. The temperature is often subnormal, although intercurrent attacks of inflammation will cause a temporary elevation. One of my cases showed many attacks in which there was a high range of temperature and considerable evidence of sepsis. A small nodular or a large smooth growth may be felt in the region of the gall-bladder, which may or may not be tender on pressure. Usually tenderness can be elicited on deep pressure, but it is less than is present after an attack of colic or an attack of acute cholecystitis. In duct cancer no tumor is to be detected unless the gall-bladder is distended, when it presents as a palpable tumor. If the hepatic ducts are occluded, the gall-bladder is small and cannot be felt. When the ducts are encroached upon, the patient becomes icteric, and this jaundice while varying from time to time rarely disappears entirely. At this time the stools will be found to be pasty and clay-colored. Ascites is not infrequently present late in the course of the disease, but none of my cases presented this symptom. The presence of ascites renders the prognosis especially grave. In many cases the right extremity of the liver is drawn downwards by the weight of a very large tumor of the gall-bladder; in two of my cases it extended almost to the iliac spine. With increasing jaundice, the patient develops a tendency to hæmorrhage which is very noticeable, and which is of the greatest importance in forming an opinion of the probable outcome of an operation, since the hæmorrhage may prove alarming or even fatal. The cholæmia becomes more and more profound and the patient finally succumbs to the poison. The symptoms of duct carcinoma, as a rule, to which, however, there are exceptions, are not preceded by a history of gall-stone colic or cholecystitis. In these cases the first symptom is jaundice, which may appear without any pain or tenderness. Later a tumor may be detected in the right hypochondrium, pear-shaped, with the lower margin free, continuous with the liver above, and moving with the diaphragm in respiration. The gall-bladder may be so distended that rupture may occur, as in a case reported by B. Huguenin.[5] The occurrence of rupture is promptly followed by acute general peritonitis and the patient dies shortly of profound sepsis. Care should be observed in the examination of these over-distended bladders lest the manipulation cause rupture.

The diagnosis is to be made by a careful consideration of the antecedent history of carcinoma in the family, and of the patient having suffered from the symptoms usual to the presence of gall-stones for a prolonged period followed by a rapid loss of weight and strength. The pallor, the jaundice, and the presence of an indurated nodular mass in this region, whether accompanied by pain or not, are strong presumptive evidence of biliary cancer. The absence of jaundice, or even of a tumor, is not an indication that carcinoma is not present. Cancer of the ducts is to be suspected when jaundice is persistent and progressive in an elderly patient who is losing flesh rapidly. The malignant growth of the ducts is usually of small size and cannot be detected, but the distended gall-bladder is often quite perceptible. To differentiate from stone in the common duct the gradual onset of jaundice is important, as most cases of common-duct stone develop jaundice very suddenly. One would think that the jaundice following the presence of a malignant tumor of the bile-duct would be constant and steadily increasing, while really many of such cases show a marked variation in the amount of jaundice, the patient being at times markedly clearer than at others. The jaundice from stone is subject to more abrupt change but may at times be as deep as that from cancer. Temperature is not a reliable guide in diagnosis between the two conditions, but the frequent occurrence of attacks of cholecystitis and cholangeitis with a sharp rise of temperature would tend to strengthen the presumption of stone. The presence of great nodulation in a tumor in this region will justify a diagnosis of malignancy. The other conditions which may confuse the observer are: tumors of the stomach, intestine, or pancreas; tumors and hydatids of the liver; hydrops of the gall-bladder from mechanical cause; and tumors of the kidney. Tumors of the stomach will almost always present a history of indigestion, nausea, vomiting, hæmatemesis, pain increased by eating, and the presence of occult blood in the stools, also the absence of jaundice. Such symptoms should be sufficient, if taken in connection with an analysis of the gastric contents and motility, to allow one to reach a conclusion. Intestinal tumors will present symptoms of obstruction, or at least of intermitting diarrhœa and constipation, with the presence of a tumor which is more movable and which does not follow the diaphragm in its excursions. It may not be possible to differentiate between tumors of the pancreas and the bile-passages, although the presence of undigested fat in the feces may prove a valuable guide. Tumors of the liver are in the larger number of cases malignant and due to extension from the gall-bladder, hence the diagnosis is unimportant except as a matter of prognosis or to determine for or against operative interference. The size of the liver and the amount of nodulation it presents will usually make the diagnosis clear, and as a rule when the growth has progressed to the extent that the surface of the liver presents palpable nodules, the case has passed beyond the aid of surgery. In hydatids of the liver the size of the organ will be greatly increased and fluctuation will usually be readily detected. Abscess of the liver will show a marked enlargement of the organ in a symmetrical way and will be accompanied by a low range of fever. Fluctuation will finally be noted, as will a certain amount of œdema over the abscess, and aspiration will make the diagnosis conclusive. Hydrops of the gall-bladder from mechanical causes will not show the marked emaciation that is present in malignant cases, and the condition which mechanically obstructs the duct will present its characteristic symptoms. Renal tumors can be differentiated by their position and by the symptoms being all referred to the urinary system, and also by a thorough examination of the urine. It is well to remember that gall-bladder growths keep well to the right side of the abdomen as they develop, and they do not always, in my experience, grow toward the umbilicus, as claimed by Musser.

The prognosis is of necessity very grave, a fatal termination being certain unless complete extirpation is done. The very nature of the condition and the structures in close relation which are so likely to be involved renders a cure even in this way very uncertain. Courvoisier recites a case of Hochenegg which had gone for eight months without a recurrence, and says it is a highly satisfactory result. Woerner mentions one in good health three years after operation. With earlier diagnosis and a wide excision of the gall-bladder and the liver-tissue it would appear probable that the prognosis would be materially improved. In cases of cancer of the duct the mortality is of necessity higher, owing to the mechanical difficulty of removing the disease and reëstablishing the communication with the intestine. When the gall-bladder is healthy and contains bile a temporary respite may be given to the patient with duct cancer by cholecystenterostomy.

The treatment may be classed as prophylactic, palliative, and radical. The first, upon which too much stress cannot be laid, consists in the recognition of the importance of early operation for gall-bladder disease and the necessity of impressing this fact upon such patients. Formerly the writer held to the belief that many cases of gall-stones should be allowed to go without operation, if the symptoms produced but little disturbance. In the light of our present knowledge, we consider that every case of this condition, in which a diagnosis can be made, should be subjected to operation if the patient's condition will safely permit. Under prophylaxis may also be included measures to prevent cholecystitis and cholelithiasis, as it appears conclusive that these conditions are largely responsible for malignant disease of the gall-bladder. Palliative treatment is to be instituted in those cases which have passed beyond the possibility of radical attack, and will consist of measures designed to give the patients as much comfort as possible, while waiting for the end. The radical treatment includes any of the surgical measures instituted for the removal of the disease or for the temporary relief of the cholæmia. The most recent investigations show that a considerable portion of the liver can be safely excised, with the technic now in use. In order to insure the least probability of a recurrence, the liver-tissue about the gall-bladder should be removed, and if the liver presents to the eye evidence of malignancy it should be more freely attacked by the surgeon. If such free attack does not appear feasible, the operation should be abandoned. The chief danger, in such procedure, lies in the difficulty of controlling hæmorrhage from the liver wound. A number of plans have been advised to overcome this danger. The elastic ligature has proven quite serviceable for the temporary arrest of hæmorrhage, and has even been advised as a permanent means of hæmostasis, the stump of the liver being left in the wound. The fixation of the stump in the abdominal wall has the disadvantage of a greater risk of sepsis, hence it is not much employed. Dr. Leonard Freeman[6] of Denver has published an article in which he mentions eleven methods of permanent hæmostasis employed by different writers. The best of these consists of sutures applied in a special manner, and the use of gauze compresses. Kurzenow and Pensky in 1886 proposed a method which, as modified by Auvray in 1897, consists of the passage of a double thread from side to side through the liver, cutting the outside loops of thread and by multiple ligation controlling the flow of blood. These ligatures may cut through the friable parenchyma but hold the blood-vessels. To prevent the ligatures cutting through the liver-tissue nothing will prove so satisfactory as a small roll of gauze over which the ligatures are passed; after the catgut is absorbed the gauze can be readily removed by slight traction upon an end which has been left in the wound. Hochenegg has already made use of gauze as a compress sutured in the liver wound, but did not make use of it in the way just mentioned. Whatever method of control may be employed, it will be found wise to place a pack of gauze over the wound in the liver to control capillary oozing. Such a pack will usually be needed in cholecystectomy for cancer to provide for drainage of the ducts.

The mortality of operations upon cases of cancer of the gall-bladder will of necessity be high,—first, because of the condition in which these patients are found when they come to the surgeon for relief; being usually anæmic, low in flesh and strength, with all the organs impaired, and very poor surgical risks. They may be suffering from jaundice of a persistent type, making the control of hæmorrhage a most serious problem. The presence of jaundice adds so much to the risks that Mayo says it contraindicates operation. Again, these patients have usually suffered for some years from the effects of gall-stone disease, hence have acquired many and dense adhesions in the region of the gall-bladder, which will add to the mechanical difficulties of the operation, thus prolonging it when everything demands that it should be completed with celerity. The hope of a permanent cure must be small when all things are considered. The primary mortality will depend largely upon the time at which these patients come for operation, and upon the surgery necessary for their relief. Mayo reports nine deaths in forty operations for malignant disease of the gall-bladder, or 22.5 per cent. Hans Kehr records a case of recovery from hepático-duodenostomy for duct cancer. Heimann gives a table showing 169 cases collected in years of 1895 and 1896 from reports of the Royal Statistical Bureau of Prussia: 147 treated, 95 died, 64.6 per cent. mortality; 42 operated, 24 died, 57 per cent. mortality.

The methods of removal of the growth and the plastic surgery necessary in these cases must be determined by the conditions met, and this field of surgery is certainly not suited to the timid operator.

From a consideration of the facts set forth in this paper it seems that failure to urge an early operation to patients suffering from disease of the gall-bladder is reprehensible, even if no other reason existed than the remote one of the late development of malignancy, while in fact there are many reasons which urge early interference which the scope of this paper does not permit us to discuss. One of the most difficult problems which arises in connection with this subject is to determine which case offers a chance for benefit to the patient by operation and which does not. Three conditions seem to us to be rather strong contraindications to interference, viz., the presence of marked jaundice, the presence of a palpable nodulation in the gall-bladder region, and ascites. As a rule either of these conditions shows that the disease has progressed beyond the aid of the surgeon. Again operation is not to be undertaken in cases which show marked defect in the urinary secretion or in the action of the cardiac and respiratory organs.

We have had opportunity to see four cases of carcinoma of the gall-bladder and ducts which have come to operation, in addition to two cases in which the operation was abandoned after the abdomen was opened, and which were not positively demonstrated as primary disease of the gall-bladder although there is every reason to believe that such was the case. Both of the latter cases had marked jaundice; in one a tumor could be felt and in the other the mass lay too deeply under the liver to allow detection by palpation. One of these patients lived for three months and the other is still alive, but the time is too short since the operation upon the last patient for the case to be of any value. Of the four primary cases two were primary of the gall-bladder and two of the ductus communis. One of the latter presented evidences of malignancy in the wall of the gall-bladder as well as in the duct, but the history clearly shows that the duct was first involved. The cases of duct cancer occurred in a colored man of sixty and a white woman of fifty-four years. The patients suffering from cancer of the gall-bladder were white, one a male of fifty-eight, the other a female of fifty-three years. Stones were present in all except that of the colored man with duct carcinoma.

CASE I. A colored man of about sixty who gave an unsatisfactory history. He was markedly jaundiced, had lost considerable flesh, his appetite was poor and the cholæmia was pronounced. A diagnosis of gall-stones was not substantiated by operation, the condition consisting of a duct cancer with a distended bladder and a small cyst of the pancreas near its tail. A cholecystenterostomy was performed, which resulted fatally as the result of an error in technique, the latter consisting in the use of a second or reënforcement suture for the Murphy button. The wall of the gall-bladder was thin and unable to stand the strain of the tension produced by this additional suture. Murphy has later advised against the use of such a suture. The specimen of growth obtained post mortem showed it to be a carcinoma of the glandular type involving the lower end of the common duct.

CASE II.—Cancer of the duct and gall-bladder. This patient was a white woman of fifty-four, whom I first saw June 17, 1903. Her father died of jaundice, probably malignant, at the age of sixty-two, one aunt died of cancer of the uterus, and one sister died in January, 1903, at the age of fifty-six, of cancer of the liver, in the same room in which I found this patient. She had washed her sister's clothes after her death, but did not wait upon her much while sick. Her sister had vomited occasionally and the room had not been thoroughly cleaned or disinfected. Her personal health had been good except for constipation until December, 1902, when she began to feel sick with pain in the right side of the abdomen, lasting two or three days. Five weeks before I saw her she had a chill, but soon improved. One week later she became nauseated, vomited, lost appetite, and became jaundiced. Soon after this a mass was felt in the right side of the abdomen. Since the appearance of this mass she has suffered very little pain, but has lost about fifteen pounds of flesh, and the jaundice has deepened. She feels fairly well with the exception of extreme weakness. On examination a smooth, firm, pear-shaped mass is found in the upper right abdomen. It is connected with the liver above and extends down along the outer edge of the rectus to within an inch of the anterior superior spine of the ilium. A probable diagnosis of cancer of the gall-bladder was made, and after a full explanation of the dangers, an exploration was advised. The urine showed a large quantity of bile, albumin and casts. The hæmoglobin percentage was 70, the white cells numbered 9000 and the red 6,880,000.

Operation June 24, 1903. The gall-bladder was greatly distended, and contained a large quantity of yellowish bile mixed with mucus, and one large and several small stones. Careful exploration of the ducts showed no other stones, but at the duodenal end of the common duct a small, hard nodule the size of a hazelnut could be felt, which was at first thought to be a stone, but careful investigation disproved this. The gall-bladder was stitched to the peritoneum and fascia of the abdominal wall and drained through a rubber tube. The patient recovered from the operation nicely and while there was a slight improvement in the jaundice it never disappeared entirely, convincing us that the original diagnosis was correct. She died December 13, 1903, in a markedly cholæmic condition. The postmortem showed the gall-bladder, which was large at the operation, to have become small, contracted and functionless save for some mucous contents. The common and cystic ducts were completely obstructed, and the former and the hepatic ducts were widely dilated and filled with bile. The liver was nutmeg in appearance, bile-stained, larger than normal, and contained in its dilated ducts a number of stones. The same nodule which was felt at operation was found slightly enlarged at the duodenal end of the choledochus, and considerable thickening and induration existed at the junction of the cystic and hepatic ducts, in the adjacent liver, and in the wall of the gall-bladder as well. Dr. John E. Hays reports the microscopical examination to show the condition to be an adenocarcinoma of the ducts and gall-bladdder.

CASE III.—Carcinoma of the gall-bladder. This patient, a white man of fifty-eight, was seen about one year ago. He gave a history of repeated attacks of gall-stone colic, but had refused operation, and his physician had exhausted the usual remedies for the relief of the condition without avail. On one occasion the patient had passed several gall-stones in the stool. Recently he had lost about forty pounds and was having attacks of fever, chills, pain, and vomiting. I found him pale, flabby-cheeked, and looking very much aged. His pulse was 50 and very feeble. A hard nodular mass could be readily felt under the right rib margin, which was only slightly tender on pressure. He was slightly jaundiced, and his urine was not favorable for surgery. A diagnosis of gall-stones was made, with strong probability of cancer of the gall-bladder. A very gloomy prognosis was given and exploration suggested as the last resort. A month later, after consulting several other gentlemen, he requested me to make the exploration, and I reluctantly consented. He was then suffering from a marked toxæmia and was running a fever of 103. No encouragement for a recovery was given the family. The operation was done under ether, which was taken badly, and a small gall-bladder completely covered with adhesions and containing no bile was removed. Three small stones were found, one lying outside the wall, one in the wall, and one inside the bladder. The patient did not stand the operation well and died at the end of twenty-four hours.

CASE IV., a white woman of 54, gives a history of repeated attacks of gall-stone colic for the past six years, with an increasing tumor in the right hypochondrium during the past year. She has been jaundiced often, vomited and suffered pain, and during the past year has lost forty pounds. The mass was globular, cystic in feel, slightly movable, and extended from the ribs to the anterior iliac spine. It simulated a hydronephrotic tumor, as the colonic resonance was internal to it. The patient had a sallow, cachectic skin, but was not icteric. A diagnosis of distended gall-bladder, possibly malignant, with stones, was made. Operation December 12, 1905, revealed a very large gall-bladder, containing a large carcinomatous mass and over forty stones, which was removed with a portion of the adjacent liver-tissue. The stump of the cystic duct was ligatured with catgut, contrary to the usual plan of treatment in these cases, as there seemed to be no necessity for drainage of the ducts. The liver was sutured with catgut and a gauze pack inserted to control oozing. She suffered from temporary suppression of urine and her condition was critical for two days following the operation, but from that time her improvement was continuous. The microscopical report shows these cases to be adenocarcinomata of the gall-bladder. The gall-bladder in the last case was almost completely filled with a soft, papilliform growth, leaving just enough room for the stones and a small amount of fluid, almost the entire wall of the gall-bladder being involved in the growth. Infiltration of the liver by the malignant tissue was shown at several points. The drawings show the gall-bladder intact and cut transversely.

Figure 1 represents a section taken from Case II, which was an adenocarcinoma of the common duct with the secondary, or coincident, involvement of the gall-bladder, which to the eye presented only the appearance of inflammatory change. Sections from this growth through the wall of the duct into the tumor proper show the wall to be invaded with adenomatous tissue. The mucous membrane of the duct itself is very little changed, but infiltrating the other coats we find a proliferation of poorly developed gland-tissue. The glands are irregular in shape and size, and are lined with a varying number of ill-formed columnar cells. The fibrous coat is thickened, and shows but little stroma between the glands. In some places the lumen of the glands is entirely filled with epithelial cells.

Figure 2.—Primary carcinoma of the gall-bladder. Case III.—This section includes the gall-bladder wall and a portion of the adjacent liver-tissue. The pathologic findings are described by Dr. John E. Hays as follows: "The liver lobules show fatty degeneration and passive congestion. The adventitious coat of the blood-vessels is very much thickened. An increase of new connective tissue in the portal canals, and an irregular distribution of the ducts, is observed. The growth in the gall-bladder is composed of an abundant stromà of connective tissue holding the new glandular structure. These glands are very much dilated, tortuous and lined with one to several layers of columnar epithelium, fairly well formed. This epithelium breaks

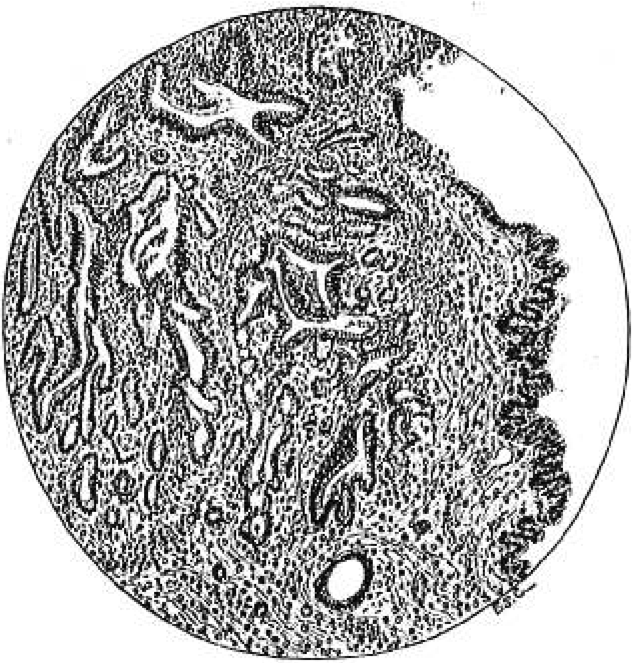

FIG. 1.—Case II.

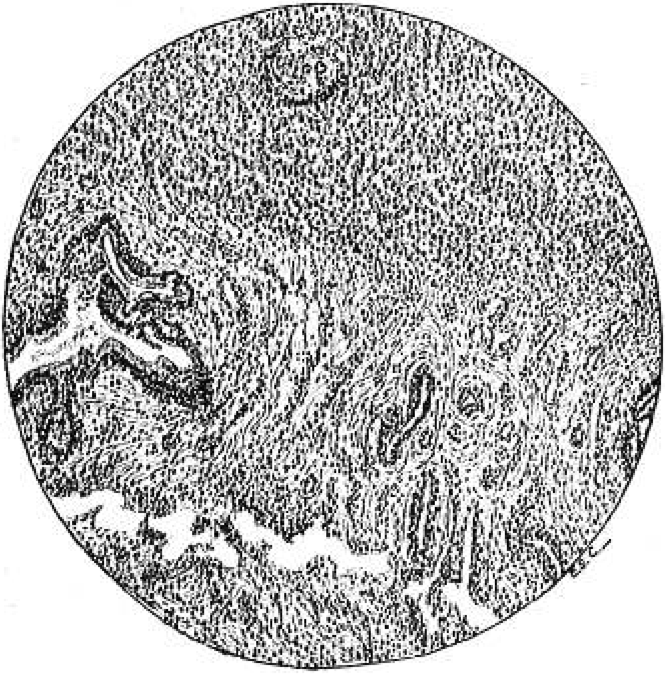

FIG. 2.—Case, III.

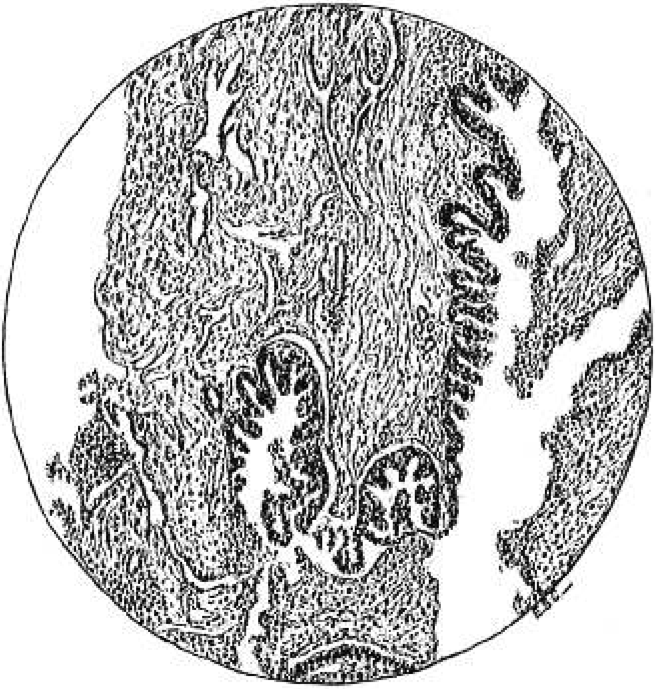

FIG. 3.—Case IV. Low power.

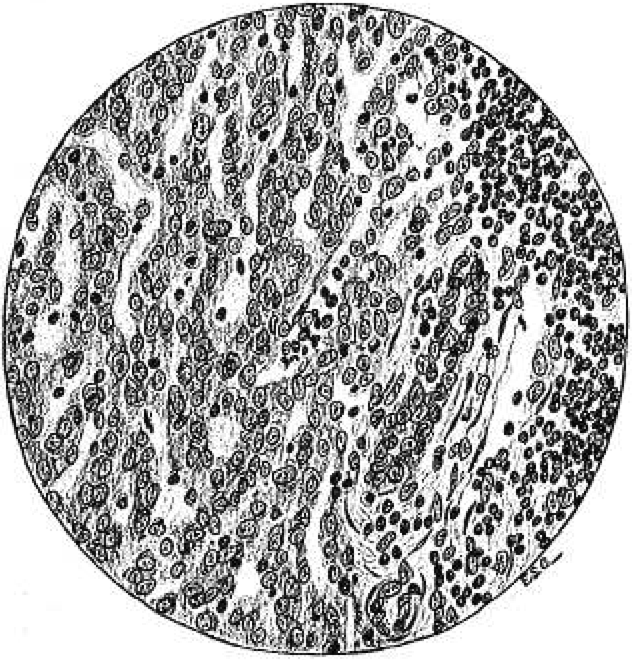

FIG. 4.—Case IV. High power.

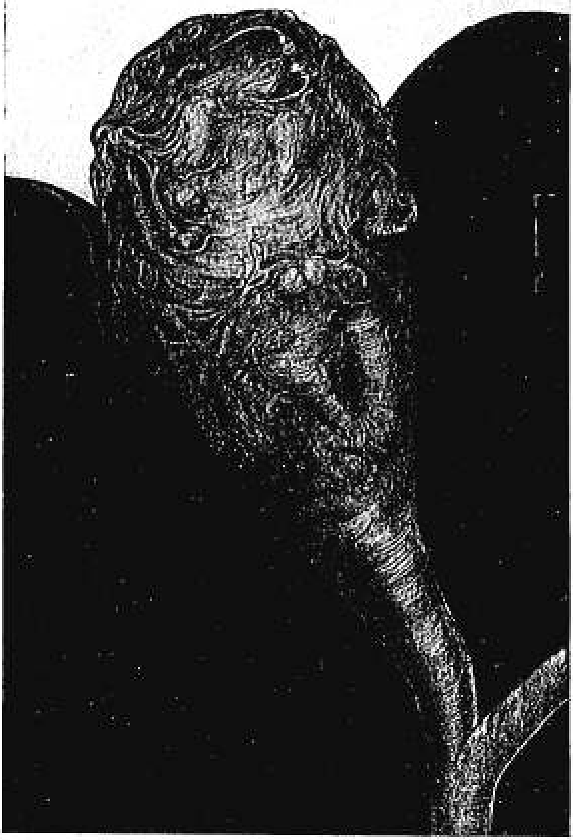

FIG. 5.—Gross appearance, Case IV.

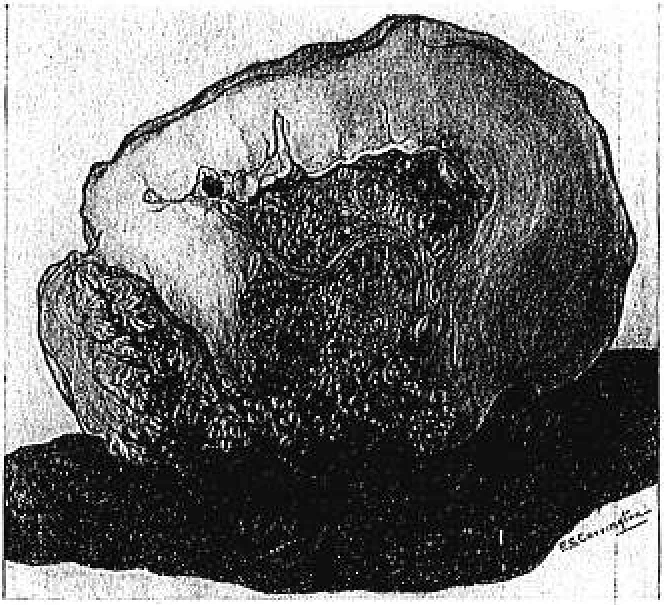

Fig. 6.—Transverse section illustrating Case IV.

through the basement membrane in places and infiltrates the surrounding stroma and liver-tissue. At one point in the section an accumulation of squamous cells is seen, and considerable round-cell infiltration of the connective tissue of the portal canals is noted."

Figures 3 and 4.—Adenocarcinoma of the gall-bladder, papilliform in type. Case IV. This section shows the neoplasm growing largely into the lumen of the gall-bladder, almost filling its cavity, and also a marked involvement of the wall of the gall-bladder throughout its entire thickness. The new growth consists of a proliferation of adenomatous tissue, papilliform in the arrangement of its glandular elements. The glands are very irregular in size and shape, and are covered with several layers of badly developed columnar epithelium, and a very small amount of stroma. The gland-tissue which invades the wall of the gall-bladder has the same structure as that within its lumen.

Figure 5.—Gross appearance of Case IV.

Figure 6.—Transverse section of same.

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